

## **REMARKS**

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

### **I. CLAIM STATUS AND AMENDMENTS**

Claims 12-22 were pending in this application when last examined.

Claims 12-16 were examined on the merits and stand rejected.

Claims 17-22 were withdrawn as non-elected subject matter.

Claim 12 is amended. Support for this amendment can be found, for example, on page 11, lines 3-13, of the specification as filed.

Claim 12 has also been amended to better conform with U.S. practice.

Thus, no new matter has been added.

### **II. FOREIGN PRIORITY**

The Examiner is respectfully requested to acknowledge the claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f) by checking the appropriate boxes in item 12 on page 1 of the next Office Action.

### **III. INDEFINITENESS REJECTION**

On page 2 of the Office Action, claims 12-16 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite for the phrase “characterized by.” This rejection has been overcome, as applied to the amended claims, for reasons which are self-evident.

### **IV. OBVIOUSNESS REJECTION**

On pages 3-7 of the Office Action, claims 12-16 were rejected under 35 U.S.C. § 103(a) as obvious over Grunert et al. (US Patent 6,010,908) and in view of Moriya (PNAS, vol. 90, pp. 1122-1126, 1993) and Marron et al. (Diabetes, vol. 49, pp. 492-499, 2000).

Grunert et al. teaches single-stranded DNA obtained by denaturing PCR products (i.e., double-stranded DNA). Therefore, the single-stranded DNA of Grunert et al. is a mixture of

both the sense and the antisense strand of the target DNA, (see the Office Action, page 4, lines 15-21).

On the other hand, as shown in the Examples and Comparative Examples of the specification, the claimed invention uses either the sense strand or the antisense strand of the target DNA. Such difference is clarified in amended claim 12. Applicants further note that claim 12 indicates that the single stranded DNA fragment was prepared from a single stranded circular DNA and thus does not contain a mixture of strands.

If a mixture of both the sense and the antisense strand is used, such strands anneal together due to base complementarity, thus inhibiting replacement of the target DNA strand. Such annealing leads to a double-stranded DNA fragment, which is substantially the same as the PCR product. Such a PCR product is much less effective in the claimed invention. Please see "Comparative Example" (page 25) and Fig. 4 of the specification.

On the other hand, use of only the sense strand or the antisense strand, as claimed, is much more effective in correction frequency than the use of PCR products (pcrHES).

Further, Grunert et al. never teaches or suggests such superior effects of use of only the sense or antisense strand. Therefore, even if Moriya et al. teaches a preparation of a single-stranded DNA fragment by using a single-stranded circular DNA, one of skill in the art would not be motivated to create the claimed invention.

Furthermore, in column 3, lines 38-47, of Grunert et al., it is taught that the use of ssDNA fragments have not been shown to achieve or demonstrate nucleotide exchange in chromatin DNA or to cause changes in cell phenotype when genes are integrated into components of genomic DNA. Also, in column 4, lines 11-15, of the same reference, the authors indicate that previous attempts to correct mutated genes were inefficient. Thus, in light of the teachings of this reference, a person of skill in the art will not be motivated to combine Grunert and Moriya et al. to arrive at the claimed invention. In fact, it is submitted that Grunert et al. teaches away from such a combination.

Thus, for the above-noted reasons, Applicants suggest that this rejection is untenable and should be withdrawn.


**CONCLUSION**

In view of the foregoing amendments and remarks, the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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